REMARKS

In the Office Action dated July 20, 2006, claims 18-34 were indicated to be rejected and claims 21 and 25 withdrawn pending allowability of a generic claim.

Applicant has amended claims 18-24, 26-28 and 32-34 to address objections recited at paragraphs 4-6 of this Office Action.

Applicant has amended the specification to insert Sequence Identifiers into the text. Applicant is unaware of any requirement to identify digests of the sequences such as found in Fig. 2B.

All claims had been rejected over various combinations of Firestone et al., (J. Controlled Release) in view of WO-A-98/10794 and U.S. Patent No. 6,1243,256.

Applicant has amended the claims, especially claim 18, to specify that the medicament uses albumin as a carrier for the carrier-drug conjugate.

The differences between the invention as now claimed and any hypothetical permutation or combination of Firestone with WO-A-98/10794 should become apparent.

Contrary to the carrier-drug conjugate describer in WO-A-98./10794, the present application relates to a carrier-drug conjugate wherein at least 0.7 mol of drug is bound via the thiol binding group to the cysteine group of the carrier (cf. amended claim 18). In particular, the examples describe *inter alia* the preparation of a conjugate in which 0.97 mol of drug is bound to the carrier (cf. for example section [0079], last sentence, of the present application). This

surprising high binding rate of the drug leads to the present application. This surprising high binding rate of the drug leads to carrier-drug conjugates having an extremely high purity of more than 95% (cf. for example section [0068], of the present application).

Moreover, the carrier-drug conjugate described in Firestone et al. is prepared by a method comprising the chemical modification of the amino acids of the carrier (cf. for example the bridging paragraph between page 252, left column, and page 253, right column, of the Firestone et al. reference) or the reduction of the internal disulfide bridges of the carrier (cf. for example page 253, left column, lines 18 to 21, of the Firestone et al. reference). This may lead to an instability and/or a change of the tertiary structure of the carrier, thus causing a deterioration of its functional characteristics including bioavailability.

To the contrary, according to the present invention, the disulfide bridges between the cysteine group of the carrier and another compound are advantageously reduced without reducing the internal cysteine bonds (cf. for example section [0062] of the present application). Thus, the present invention is based on a completely different and superior concept for reducing the carrier and minimizes the dimensional changes in the remainder of the peptide.

Furthermore, according to the present invention, the spacer molecule and/or the linkage between the different components of the drug can be selected such that tit is hydrolytically and/or enzymatically cleavable (cf. amended claim 18). This enables the separation of the carrier from the pharmaceutically and/or diagnostically active compounds at the place of action or target organ. This

surprisingly effective targeted and rapid release of the active compounds from the carrier using an enzymatically cleavable linkage is shown e.g. in the examples of the present application (cf. for example section [0087] and Fig. 2A and 2B of the present application).

In this context, it is noted that the Firestone et al. reference does not teach or suggest carrier-drug conjugates which comprise components being connected via enzymatically cleavable linkages.

A further advantage of the claimed medicament comprising a carrier-drug conjugate is the fact that the active compound can reach the place of action very specifically (high specificity). Thus, the claimed medicament can simply be injected into the blood vessels (cf. for example section [0014], 2nd and 3rd sentence, of the present application). This leads to surprisingly good results in *in vivo* experiments (cf. for example section [0091], Table 2, and Figs. 3A and 3B of the present application). This meets the threshold for utility which a reviewed paper, such as Firestone's, need not meet.

In view of the above, the subject matter defined in amended claim 18 of the present application is believed to be non-obvious in view of the cited prior art. The same applies *mutatis mutandis* to the subject matter of amended directly or indirectly dependent claims 19 to 34 of the present application.

The Narazaki reference requested by the Examiner was cited in another patent office and is not available immediately to the undersigned or his German associated.

Respectfully submitted,

J. Herbert O'Toole
Registration No. 31,404
Attorney for Patentee
NEXSEN PRUET, LLC
P.O. Box 10107
Greenville, SC 29603
Telephone: 864/ 370- 2211
Facsimile: 864/ 282-1177

Attachments: 1) Page 25; 2) Statement

I hereby **CERTIFY** that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope address to: Commissioner for Patents, P.O. Box 1450, Alexandria VA 22313-1450

Date: Oct 20 2006 by: Jacqueline Beavers